REMARKS

This Amendment is in response to the December 3, 2008 Office Action ("Office Action") and Advisory Action of February 9, 2009.

Applicants would like to thank the Examiner for conferring with Applicants' representative Jennifer Theis on December 8, 2008 and on December 29, 2008. The Examiner clarified that item #6 on page 3 of the Office Action should refer to the pending claims 44-78 rather than 4-38. The Examiner also clarified that item #6 on page 3 of the Office Action should refer to the April 8, 2008 1.132 declaration filed rather than the October 30, 2007 declaration. Additionally, the Examiner admitted that pyroglutamic acid is equivalent to the sodium salt of pyrrolidine carboxylate as stated in the Amendment filed April 8, 2008. No agreement was reached as to the status of the claims.

Applicants respectfully disagree with the Examiner's position that the showing of the declaration is not commensurate with the scope of the claims as amended as of April 8, 2008. Claim 44, as amended, discloses broad compositions of gluconic or pyroglutamic acid, a short chain anionic surfactant and a calcium ion scavenger that may be citric acid, malic acid, succinic acid, or polyacrylic acid. As the examiner admitted in the December 8, 2008 interview, pyroglutamic acid is equivalent to the sodium salt of pyrrolidine carboxylate. As the claim reads, the compound includes citric acid or malic acid. Taking these two factors into account, the only example in the April 8, 2008 1.132 declaration that does not fall within claim 44 is Example 9. Examples 1-8 and 10-12 are within the scope of claim 44, and therefore the declaration is commensurate with the scope of the claims and should be given ample patentable weight.

The remaining independent claim, claim 44, has been amended to limit the composition to one that is capable of inactivating viruses including one of at least rotavirus, coronavirus, respiratory syncytial virus ("RSV"), and combinations thereof. Support for this amendment is found at page 3, lines 30-32; page 4, lines 15-16 and 31-33; page 5, lines 21-23; page 6, lines 7-10 and 31-33; page 15, lines 8-10; page 16,

lines 9-13; page 18, lines 25-34; page 19, lines 1-3, 7-12, and 16-19; page 25, lines 5-27; Tables 4 and 5; and in claims 30-31 as originally filed.

Claim Rejections

In the present Office Action, claims 44-78 stand rejected under 35 U.S.C. § 102(b) as anticipated by, or in the alternative under 35. U.S.C. § 103(a) as obvious over U.S. 2002/0098159 to Wei, et al. ("Wei"). In addition, claims 44-78 stand rejected under 35 U.S.C. § 102(b) as anticipated by U.S. Pat. No. 6,190,675 to Beerse, et al. ("Beerse"). Claims 44-78 also stand rejected under 35 U.S.C. § 103(a) as obvious over Beerse. Applicants have overcome these rejections by amending claim 44, as discussed in detail below. Claim 72 has been canceled. Applicants respectfully request that the Examiner allow claims 44-71 and 73-78.

1. General Remarks

The present rejections involve two references: Wei and Beerse. Wei teaches compositions comprising surfactants, including anionic surfactants, cationic surfactants and/or zwitterionic or amphoteric surfactants, and organic and/or inorganic acids, where the pH of the compositions is less than 5. Wei states that the compositions are effective for inactivating viruses, but merely discloses effectiveness for rhinovirus – not the claimed viruses. Beerse merely discloses compositions that are effective against Gram-positive bacteria and fails to mention effectiveness against viruses. In fact, Beerse's teaching that the anionic surfactant action allows the antimicrobial active into the cell wall teaches away from use for viruses because viruses are not cells and have no cell wall or cell membrane. Beerse, col. 8, ll. 24-32; *See* George F. Brooks et al., *Jawetz, Melnick & Adelberg's Medical Microbiology* 2 2004 (attached as Exhibit A). Viruses are not bacteria and the methods of inactivating viruses are different than the methods of killing bacteria. *See* Günter Kampf and Axel Kramer, *Epidemiologic Background of Hand Hygiene and Evaluation of the Most Important Agents for Scrubs and Rubs*, Clin. Microbiol. Rev.,17: 863-893, 868, 871-80. (2004) (attached as Exhibit B).

There are different types of viruses, including enveloped, which have an outer lipid envelope surrounding a protein coat and an inner core of nucleic acid, and non-

enveloped, which lack a lipid envelope around the protein coat and inner core of nucleic acid. J. Owen Hendley et al., *Evaluation of Virucidal Compounds for Inactivation of Rhinovirus on Hands*, Antimicrobial Agents and Chemotherapy, 14(5) 690-94, 693 (1978) (attached as Exhibit C). Rhinovirus is a non-enteric, non-enveloped virus in the *Picornaviridae* family; rotavirus is an enteric, non-enveloped virus in the *Reoviridae* family; and coronavirus and RSV are non-enteric enveloped viruses in two further distinct families of Viridae. *See Id.*; *About Rotavirus*, Center for Disease Control and Prevention 2007, available at http://www.cdc.gov/rotavirus/about_rotavirus.htm (attached as Exhibit D); Cornelis A. M. de Haan et al., *Coronavirus Particle Assembly: Primary Structure Requirements of the Membrane Protein*, J. Virology, 72(8): 6838-6850, 6838 (1998) (attached as Exhibit E); Lewis H. McCurdy and Barney S. Graham, *Role of Plasma Membrane Lipid Microdomains in Respiratory Syncytial Virus Filament Formation*, J. Virology, 77(3): 1747-1756, 1747 (2003) (attached as Exhibit F).

Not all antibacterials are effective against viruses. Triclocarban is active against Gram-positive bacteria and is thought to act by destroying the semipermeable character of the bacterial cytoplasmic membrane. Gerald McDonnell and A. Denver Russell, *Antiseptics and Disinfectants: Activity, Action, and Resistance*, Clinical Microbiol. Review, 12(1): 147-179, 153 (1999) (attached as Exhibit G). Quaternary ammonium compounds have some effect on enveloped viruses. *Id.* at 157. Benzalkonium chloride is a known quaternary ammonium antibacterial that alone is ineffective against enveloped viruses but is partially effective against the non-enteric, non-enveloped virus genera rhinovirus. Hendley et al., *supra* at 693 (attached as Exhibit C). Ethanol has demonstrated weak activity against certain enteric non-enveloped viruses, including rotavirus and the human norovirus surrogate feline calicivirus (FCV). David R. Macinga et al., *Improved Inactivation of Nonenveloped Enteric Viruses and Their Surrogates by a Novel Alcohol-Based Hand Sanitizer*, App. Envion. Microbiol., 74 (16): 5047-5052, 5048-49 (2008) (attached as Exhibit H); *see also* Centers for Disease Control and Prevention. Guideline for Hand Hygiene in Health-Care Settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force, MMWR 2002; 51 (No. RR-16): 8-10 (hereinafter "MMWR 2002 (No. RR-16)") (attached as Exhibit I).

The variation in the effectiveness of compounds or compositions against viruses is likely a result of the variation in the structure and type of virus. However, the compositions of the present invention have demonstrated effectiveness in inactivating viruses, including one of at least rotavirus, coronavirus, RSV, and combinations thereof. None of the cited art, alone or in combination, disclose or suggest such broad antiviral effectiveness.

2. The Rejection of Claims 44-78 Under 35 U.S.C. § 102(b) as Anticipated by Wei.

Claims 44-78 stand rejected under 35 U.S.C. § 102(b). As amended, Applicants respectfully disagree with this rejection.

Wei does not teach compositions that inactivate one of at least rotavirus, coronavirus, RSV, and combinations thereof. Wei instead teaches compositions comprising surfactants, including anionic surfactants, cationic surfactants and/or zwitterionic or amphoteric surfactants, and organic and/or inorganic acids, where the pH of the composition is less than 5. *See* Wei, p. 2, paragraphs [0013]-[0015], [0020], and [0045]. Wei purports to have antimicrobial effectiveness against bacteria. However, only effectiveness against Gram-negative bacteria, specifically *E. coli*, is assessed. *See* Wei, p. 15, paragraph [0350]. Wei does not disclose a composition as taught by independent claim 44, that is capable of killing bacteria and inactivating viruses including one of at least rotavirus, coronavirus, RSV, and combinations thereof.

The Examiner argues that Wei teaches that the phrase "antimicrobial composition" as used in Wei refers to compositions used to inactivate, destroy or kill microorganisms and further that Wei teaches a "method of providing immediate inactivation or destruction of a susceptible virus..." *See* Wei, p. 2, paragraph [0023] (emphasis added). However, nothing in Wei suggests effectiveness against viruses other than rhinovirus, specifically rotavirus, coronavirus, and RSV. As well-known in the art discussed herein, rhinovirus is a particular susceptible virus. *See* Ronald B. Turner and J. Owen Hendley, *Virucidal Hand Treatments for Prevention of Rhinovirus Infection*, J. Antimicrobial Chemotherapy, 56, 805-807, 806 (2005) (attached as Exhibit J); Hendley et al., *supra* at 693 (attached as Exhibit C).

The Examiner relies on a cursory examination of the general language of a few claims. When Wei's specification is actually analyzed, it is obvious that only rhinovirus effectiveness is disclosed. Furthermore, Wei specifies certain optional components in each example that give rise to the Wei compositions' antiviral effectiveness. For example, at paragraph [0091], Wei states that "[f]or purposes of this invention the term 'aqueous component' refers to any material consisting essentially of, or predominantly of water, water soluble alcohol(s) such as ethanol, propanol or isopropanol, and mixtures thereof." These specific alcohols are potent known antibacterials, especially when mixed with at least 5-10% water. *See* MMWR 2002; 51 (No. RR-16): 8 (attached as Exhibit I).

Moreover, Examples 2-7 of Wei disclose formulations that do not support the broad antiviral efficacy of Wei's claims. Of the six examples, only one includes an anionic surfactant (Example 4, ammonium lauryl sulfate).[1] After a proper analysis of the examples of Wei, it is clear that only Example 4 is relevant to the present claims. Example 4 contains not only a known antibacterial in benzalkonium chloride, but also 10% ethanol, another potent antimicrobial. Compositions containing high percentages of alcohol are well-known to have some effectiveness against non-enteric, non-enveloped viruses, such as rhinovirus but not against enteric, non-enveloped viruses such as rotavirus. *See* Turner and Hendley, *supra at* 806 (attached as Exhibit J). Additionally, benzalkonium chloride is known to be partially effective against rhinovirus, but not other non-enteric, non-enveloped viruses. *See* Hendley et al., *supra* at 693 (attached as Exhibit C). There is no teaching or suggestion that Example 4, or any example in Wei, would have effectiveness against an enteric, non-enveloped virus such as rotavirus.

Example 4 does not disclose a composition of an anionic surfactant and an organic acid that is effective against a multitude of types of viruses. At most, all it demonstrates is that a combination of two known antibacterials is effective for inactivating the well-known susceptible rhinovirus. Asserted claims by themselves are not prior art. *See* MPEP 2121.01 "The disclosure in an assertedly anticipating reference

[1] Example 8 is a disinfecting spray including lauramine oxide, an amphoteric surfactant, and 55% ethanol, a potent antimicrobial. It does not include an anionic surfactant.

must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient..."(emphasis added) (citing *Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research*, 346 F.3d 1051, 1054 (Fed. Cir. 2003)).

Additionally, Wei's antiviral index is defined using only rhinovirus (ATCC VR-284). *See* Wei, p. 2, paragraphs [0004]-[0007] and p. 15-16, paragraphs [0333]-[0350]. Rhinovirus is a member of the family *Picornaviridae*, a family that is known to be susceptible to acids and that are inactivated at pH < 3.6. *See Rhinovirus – Material Safety Data Sheets*, Public Health Agency of Canada (2001), http://www.phac-aspc.gc.ca/msds-ftss/msds126e-eng.php (hereinafter "MSDS") (attached as Exhibit K); Hendley, et al., *supra* at 693 (attached as Exhibit C). Other enteric members of the *Picornaviridae* family are not acid susceptible. *See* Turner and Hendley, *supra* at 806 (attached as Exhibit J). Every example in Wei except Example 3 has a pH of 3. Further, Example 3, which is essentially Example 2 at a pH of 4, also contains 10% ethanol and 0.1% benzalkonium chloride. Again, rhinovirus is known to be partly inactivated by benzalkonium chloride, which has an enhanced effect in the presence of ethanol. *See* Hendley et al., *supra* at 693 (attached as Exhibit C).

The sole example in Wei that lacks a traditional antimicrobial active was tested only against rhinovirus. Wei, p. 20, paragraph [0438]. Example 8 comprises pyrrolidone carboxylic acid, lauramine oxide, and 55% ethanol. *Id.* It is unsurprising that the composition listed in Example 8 has some effectiveness against rhinovirus because the composition contains 55% ethanol. As previously noted, compositions containing high percentages of alcohol are well-known to have some effectiveness against rhinovirus, but are less effective against enteric, non-enveloped viruses such as rotavirus. *See* Turner and Hendley, *supra* at 806 (attached as Exhibit J). Furthermore, compositions containing high percentages of alcohol are also known to have little effectiveness on other enteric, non-enveloped viruses from the same family as rhinovirus, *Picornaviridae*, such as hepatitis A and poliovirus. *See* MMWR 2002; 51 (No. RR-16): 9-10 (attached as Exhibit I). Although the composition disclosed in Example 8 shows some antiviral activity, the composition does not anticipate amended claim 44 because the composition does not contain an anionic surfactant. Lauramine

oxide, or lauryldimethylamine oxide, is an amphoteric or zwitterionic surfactant. *See* Wei, p. 6, paragraphs [0072] and [0075]. Therefore, Example 8 in Wei does not show that a composition of anionic surfactants and organic acids has broad antiviral effectiveness.

Notably, the claims of the present application relate to a composition that can inactivate both enveloped viruses such as coronavirus and RSV as well as non-enveloped enteric viruses such as rotavirus. Based on an analysis of the art, there is no teaching of such broad viral effectiveness in Wei and/or Beerse. The Examiner has simply taken a top level view of a few claims of Wei and expanded the disclosure of a few terms to cover what is presently claimed.

Accordingly, Applicants respectfully submit that claims 44-71 and 73-78 are not anticipated by Wei.

3. Rejection of Claims 44-78 Under 35 U.S.C. § 103(a) as Obvious in View of Wei.

As explained above, claims 44-78 are not anticipated by Wei, nor are they obvious in view of Wei.

All of the examples disclosed by Wei teach a composition at a pH of 3 (Examples 2, 4-8) to 4 (Example 3) tested against rhinovirus only. *See* Wei, Examples 2-8, p. 19, paragraph [0436] and p. 20, paragraph [0438]. Rhinovirus is a non-enteric, non-enveloped virus, is known to be acid sensitive and inactivated at any pH below 3.6. *See* MSDS, *supra* (attached as Exhibit K). It is therefore unsurprising that each of these examples showed antiviral effectiveness against rhinovirus. There is no teaching or suggestion by Wei that its compositions would have effectiveness against rotavirus, coronavirus , and RSV.

Furthermore, only Example 8 in Wei teaches a composition of a surfactant and organic acid without an antimicrobial active. However, Example 8 teaches the use of an amphoteric or zwitterionic surfactant. There is no suggestion that the use of an anionic surfactant in Example 8 would yield the same result. Additionally, studies have shown that ethanol possesses relatively weak activity against certain enteric non-enveloped viruses, including rotavirus and the human norovirus surrogate feline calicivirus (FCV). Macinga et al., *supra* at 5048-49 (attached as Exhibit H). Therefore, the composition of

Example 8 in Wei would not be expected to inactivate rotavirus. Further, the fact that no anionic surfactant composition lacking an antimicrobial active was tested reveals that the specific short chain anionic surfactants in the claims of the present application and the antibacterial and antiviral effectiveness of such compositions are not obvious. *See* Wei, p. 3, paragraph [0045]. This is further supported by Dr. Lynch's declaration of April 8, 2008.

There is no evidence that one skilled in the art would find a composition comprising the organic acid of pyroglutamic acid or gluconic acid, a short chain anionic surfactant mixture, and a calcium ion scavenger, where the composition is characterized by a pH of from about 2.0 to about 4.5, as taught by independent claim 44, would be capable of inactivating viruses including one of at least rotavirus, coronavirus, RSV, and combinations thereof. Accordingly, Applicants respectfully submit that claims 44-71 and 73-78 are not obvious in view of Wei.

4. The Rejection of Claims 44-78 Under 35 U.S.C. § 102(b) as Anticipated by Beerse.

Claims 44-78 stand rejected under 35 U.S.C. § 102(b). As amended, claim 44 requires antiviral activity against one of at least rotavirus, coronavirus, and RSV.

The Examiner argues that Beerse anticipates the present claims because the compositions of Beerse are the same as or similar to compositions of the claimed invention and would inherently perform the same function and have similar characteristics. In order to establish a prima facie case of anticipation by inherency, the Examiner "must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). However, the Examiner would be unable to do so because the compositions of the present invention are not the same or identical as those disclosed in Beerse. The compositions of amended claim 44 comprise an organic acid, a short chain anionic surfactant and a calcium ion scavenger. Beerse discloses compositions that have either citric acid, succinic acid, salicylic acid, lauric acid, lactic acid, palmitic acid, and malic acid, but none of the compositions exemplified in Beerse combine the specific organic acids and calcium ion scavengers required by amended

claim 44 and the claims depending therefrom. Specifically, none of compositions exemplified in Beerse combine either of the organic acids, gluconic acid and pyroglutamic acid, as required by amended claim 44, with the specific calcium ion scavengers, citric acid, malic acid, succinic acid, or polyacrylic acid, as also required by amended claim 44.

Furthermore, there is absolutely no teaching in Beerse of compositions capable of inactivating viruses, nor is it reasonable to assume that the compositions of Beerse are effective against viruses. Tellingly, Beerse teaches compositions that provide improved "residual effectiveness against Gram positive bacteria." (emphasis added) Beerse, col. 1, ll. 14-15. *See also* Beerse, col. 3, ll. 18-20 and ll. 26-32 ("The term 'anti-microbial composition' as used herein means a composition suitable for application to a surface for the purpose of removing dirt, oil, and the like which additionally controls the growth and viability of transient Gram positive bacteria.") Beerse further teaches that the effectiveness of the composition against bacteria is accomplished by the anionic surfactant and the antimicrobial active:

> "[w]ithout being limited by theory, it is believed that the anionic surfactant disrupts the lipid in the cell membrane of the bacteria. The particular acid used herein reduces the negative charges on the cell wall of the bacteria, crosses through the cell membrane, weakened by the surfactant, and acidifies the cytoplasm * 2! [sic] of the bacteria. The antimicrobial active can then pass more easily through the weakened cell wall, and more efficiently poison the bacteria."

Beerse, col. 8, ll. 24-32. This is further evidence that only bacterial effectiveness is contemplated by Beerse, and in fact viral effectiveness is actually taught away from, because viruses are not cells and have no cell wall or cell membrane. *See* Brooks et al., *supra* at 2 (attached as Exhibit A).

On page 2 of the Office Action, the Examiner states that it would have "been obvious to the skilled artisan to produce the claimed composition, as the reference teaches each of the claimed ingredients, within the claimed proportions, for the same utility." (emphasis added) Beerse does not teach the same utility. Beerse says nothing of antiviral effectiveness. Viruses are not bacteria and the methods of inactivating

viruses are different than the methods of killing bacteria. *See* Kampf and Kramer, *supra* at 868, 871-80 (attached as Exhibit B).

Accordingly, Applicants respectfully submit that claims 44-71 and 73-78 are not anticipated by Beerse.

5. The Rejection of Claims 44-78 Under 35 U.S.C. § 103(a) as Obvious in View of Beerse.

As explained above, these claims are not anticipated by Beerse. Nor are they obvious in view of Beerse.

As discussed above, it would not have been obvious to the skilled artisan to produce the claimed composition because Beerse does not disclose or suggest viral effectiveness. Rather, Beerse evaluates the effectiveness of the composition against a single type of bacterium, *Staphylococcus aureus*, which is a Gram-positive bacteria. *See* Beerse, col. 21, ll. 36-39 and col. 25, l. 7. Beerse fails to provide an example (or disclosure) that its compositions are effective against any virus, much less the claimed viruses.

Each of the Examples disclosed by Beerse contain an antimicrobial active, such as Triclosan® (in Examples 1, 2, and 4-6 for shower gel; bar soap; and liquid laundry detergent), para-chloro-meta-xylenol (in liquid dish detergent), Triclocarban® (in Example 2 for shower gel), thymol oil (in Examples 3, 5, and 6 for shower gel), pyrithione zinc (in hair shampoo), and o-phenylphenol (in hand surface cleaner). *See* Beerse, cols. 31-34. Beerse recognizes that its composition is formulated by "using known antimicrobial actives in combination with specific organic acids and/or inorganic acids as proton donating agents, and specific anionic surfactants, all of which are deposited on the skin." Beerse, col. 2, ll. 56-59 (emphasis added). Beerse further discloses that "[t]he exact amount of antibacterial active to be used in the compositions will depend on the particular active utilized since actives vary in potency." Beerse, col. 4, ll. 63-65. (emphasis added).

Therefore, as discussed above, the Examiner's suggestion that the claims of the present invention are not patentable because the discovery of the previously unappreciated property of antibacterial and antiviral effectiveness is inherently present in the prior art composition is incorrect because the present application does not claim

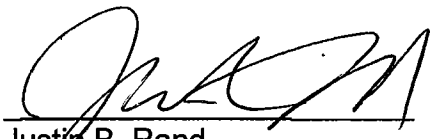
the prior art composition. There is no teaching or suggestion that the specific organic acids and/or inorganic acids and specific anionic surfactants of Beerse would have antibacterial and antiviral effectiveness at all, much less in the absence of a known antibacterial active. Further, as discussed above, not all antibacterials are effective against viruses. Thus, there is no suggestion of, nor would one of skill in the art expect, antiviral effectiveness of such a composition.

There is no evidence that one skilled in the art would expect that a composition containing the organic acid of pyroglutamic acid or gluconic acid, a short chain anionic surfactant mixture, and a calcium ion scavenger, where the composition is characterized by a pH of from about 2.0 to about 4.5, as taught by independent claim 44, would be effective for inactivating viruses. Accordingly, Applicants respectfully submit that claims 44-71 and 73-78 are not obvious in view of Beerse.

SUMMARY

Applicants respectfully request the Examiner grant allowance of this application. The Examiner is invited to contact the undersigned attorneys for Applicants via telephone if such communication would expedite this application.

Respectfully submitted,



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